Autopsy Case Reports

Image in focus

Krukenberg tumor

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How to cite: Lyngdoh BS, Dey B, Mishra J, Marbaniang E. Krukenberg tumor. Autops Case Rep [Internet]. 2020 Apr-Jun; 10(2):e2020163. https://doi.org/10.4322/acr.2020.163

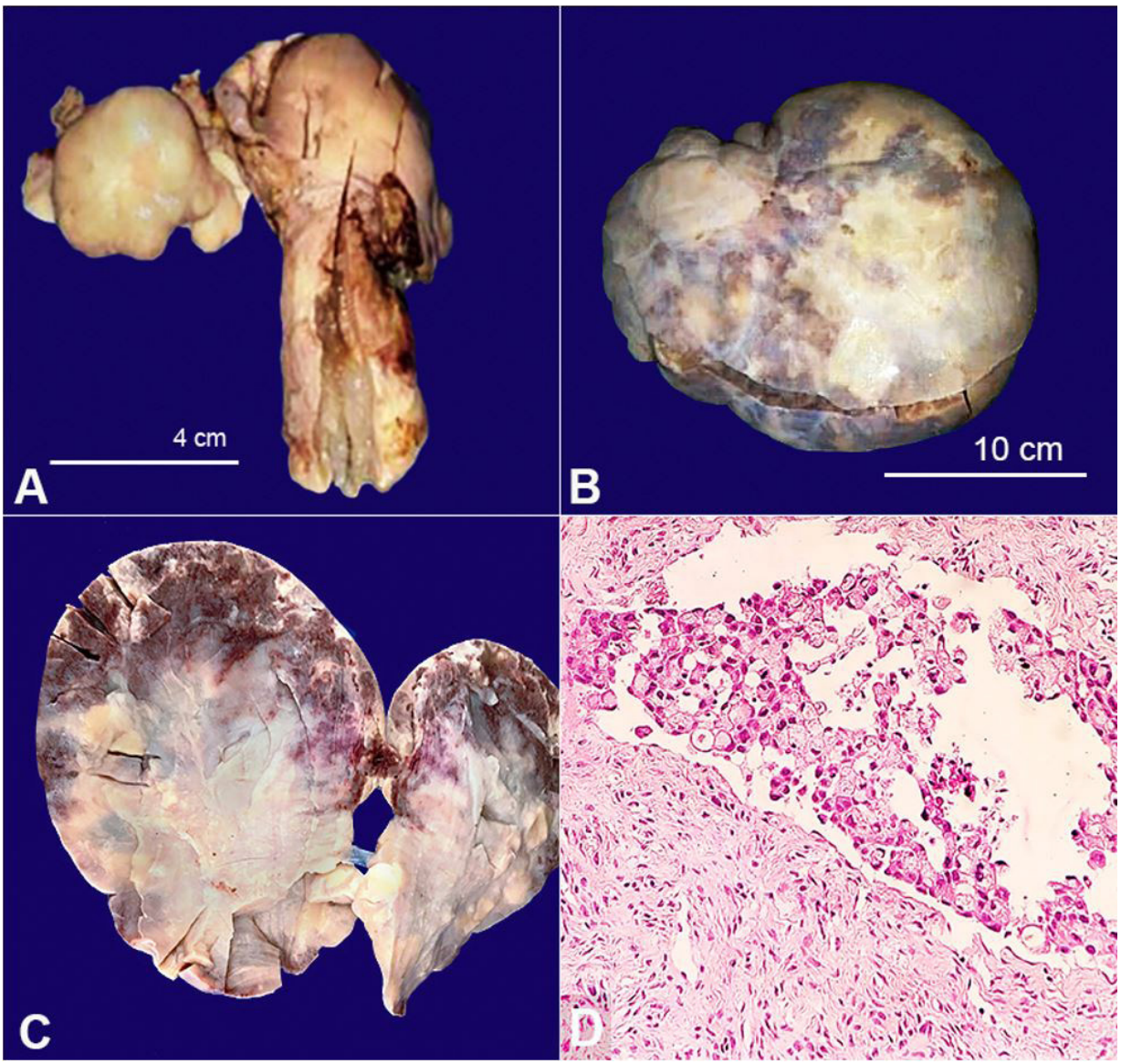

Figure 1. The external surface of both **A** – the right ovary and **B –** the left ovary was bosselated; **C** – The cut surface of the left ovary was solid, whitish with foci of congestion; **D** – Photomicrograph of the ovary showing signet ring cell adenocarcinoma (H&E, 400X).

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First described in 1896 by Friedrich Ernst Krukenberg (1871-1946), Krukenberg tumor is a metastatic signet ring cell adenocarcinoma of the ovary.[1] The incidence of Krukenberg tumors varies from 1% to 21%.[2,3] The most common primary tumor sites metastasizing to ovaries include stomach usually arising in the pylorus followed by colorectal, breast, and appendix.[1] The stomach has been attributed as the primary site in about 70% of cases.[4] Krukenberg tumor is more prevalent in Asian countries, which have a higher prevalence of gastric carcinoma.[1]

There are no apparent differences between the symptoms arising from primary and secondary ovarian malignancies. Krukenberg tumors remain asymptomatic until very advanced. In some cases, the features are non-specific, like abdominal pain, weight loss, and increasing abdominal girth.[1] The age profile of these patients is relatively younger than patients with other metastatic carcinomas.[1] This may be attributed to the higher frequency of gastric signet ring cell carcinoma in younger females.[1]

Mechanisms of the spread of Krukenberg tumor proposed are retrograde lymphatic dissemination involved in gastric cancer metastases, hematogenous spread most frequent in colorectal cancer, and transperitoneal direct spread.[5]

Radiologically, Krukenberg tumors appear as complex semisolid masses with varying proportions of solid and cystic components.[6] Secondary lymphomatous involvement of ovary usually from the upper gastrointestinal tract is solid, whereas colonic primaries are predominantly cystic in nature.[6] Metastases from breast primaries to the ovaries tend to be of small size.[6] Among all the other imaging characteristics of Krukenberg tumors, bilateral involvement of the ovaries appears to be the most helpful finding in differentiating from primary ones with over 80% of them being bilateral in nature.[4,6]

Grossly, Krukenberg tumors are asymmetrically enlarged with bosselated contour.[1,4] Microscopically, they are signet ring cells adenocarcinomas accounting for at least 10% of the tumor.[2] IHC plays an important ancillary method in confirming the diagnosis. The most commonly used IHC markers are CK7, and CK20.[1] Metastatic gastric carcinomas are CK7 and CK20 positive in 55%, and 70% of cases, respectively.[7] Colorectal carcinomas are usually negative for CK7 but positive for CK20 in most cases.[7] In contrast, primary ovarian carcinomas are almost always positive for CK7 and usually negative for CK20.[1,7] Thus, a combination of $CK7^{+}/CK20^{-}$ favors a primary ovarian carcinoma, whereas an immunophenotype of $CK7^{-}/CK20^{+}$ or $CK7^{+}/CK20^{+}$ favors a Krukenberg tumor metastasis from the gastrointestinal tract.[1,7] Positive IHC for MUC5AC suggests gastric primary.[8]

Krukenberg tumor must be differentiated from ovarian tumors showing signet-ring cells morphology and filled with either mucinous or non-mucinous material.[8] Primary mucinous ovarian carcinomas and mucinous carcinoid tumors are the important differential diagnoses for tumors with signet-ring cells filled with mucin.[8] Primary mucinous ovarian tumors have a complex papillary pattern and are usually unilateral.[9] IHC for chromogranin and synaptophysin help in ruling out mucinous carcinoid.[9] Ovarian signet-ring stromal tumor, sclerosing stromal cell tumor and clear cell adenocarcinoma are the differential diagnoses for tumors that can contain signet-ring cells filled with non-mucinous material.[9] Usually, these tumors are non-reactive for AB-PAS stain.[9]

The various unfavorable prognostic factors in Krukenberg tumors include peritoneal involvement, synchronous presentation, ascites, and increased serum carcinoembryonic antigen (CEA) levels.[10] Krukenberg tumors are stage IV disease and have a poor prognosis with a median survival of 14 months.[4]

Figure 1 represents the surgical specimen of a total abdominal hysterectomy with bilateral salpingo-oophorectomy from a 35-year-old female that was hospitalized with the working diagnosis of bilateral malignant adnexal masses. On gross examination, the uterus, along with the cervix, measured 9.5 cm at its longest axis with asymmetrically enlarged ovaries. The right ovarian mass measured 5 cm in the largest dimension, and the left ovary measured 23 cm in the largest dimension. The external surface of both ovaries was bosselated (Figure 1A and 1B). The capsules were intact and smooth without any adhesions or deposits. The attached fallopian tubes were uninvolved. On cut surface, both ovaries were solid, whitish, and with foci of congestion (Figure 1C).

Microscopic examination revealed infiltrating signet ring cell adenocarcinoma (Figure 1D). Alcian blue in the combination with Periodic acid-Schiff (AB-PAS) at pH 2.5 highlighted the cytoplasmic mucin in the signet ring cells. Immunohistochemistry (IHC) performed

showed tumor cells positive for cytokeratin 20 (CK20) and MUC5AC. The tumor cells were negative for cytokeratin 7 (CK7), chromogranin, and synaptophysin.

Upper gastrointestinal endoscopy revealed an ulcer measuring 2 cm in diameter in the greater curvature, a biopsy from which confirmed a diagnosis of signet ring cell carcinoma. Thus, a final diagnosis of the Krukenberg tumor was made.

REFERENCES

1. Al-Agha OM, Nicastri AD. An in-depth look at Krukenberg tumor: an overview. Arch Pathol Lab Med. 2006;130(11):1725-30. PMid:17076540.
2. Nakamura Y, Hiramatsu A, Koyama T, Oyama Y, Tanaka A, Honma K. A Krukenberg tumor from an occult intramucosal gastric carcinoma identified during an autopsy. Case Rep Oncol Med. 2014;2014:797429. http://dx.doi.org/10.1155/2014/797429. PMid:25386374.
3. Chanu SM, Dey B, Raphael V, Panda S, Khonglah Y. Clinicopathological profile of ovarian cysts in a tertiary care hospital. Int J Reprod Contracept Obstet Gynecol. 2017;6(10):4642-5. http://dx.doi.org/10.18203/2320-1770.ijrcog20174456.
4. Aziz M, Kasi A. Cancer, krukenberg tumor. Treasure Island (FL): StatPearls Publishing; 2020.
5. Shah B, Tang W, Karn S. An up-to-date understanding of the "Krukenberg Tumor" mechanism. Adv Reprod Sci. 2016;4(02):31-6. http://dx.doi.org/10.4236/arsci.2016.42005.
6. Karaosmanoglu AD, Onur MR, Salman MC, et al. Imaging in the secondary tumors of the ovary. Abdom Radiol (NY). 2019;44(4):1493-505. http://dx.doi.org/10.1007/s00261-018-1809-4. PMid:30361868.
7. Park SY, Kim HS, Hong EK, Kim WH. Expression of cytokeratins 7 and 20 in primary carcinomas of the stomach and colorectum and their value in the differential diagnosis of metastatic carcinomas to the ovary. Hum Pathol. 2002;33(11):1078-85. http://dx.doi.org/10.1053/hupa.2002.129422. PMid:12454811.
8. Fazzari C, Fedele F, Pizzi G, Crisafulli C, Parisi A, Caruso RA. Krukenberg tumour of the ovary: a case report with light microscopy, immunohistochemistry and electron microscopy study. Anticancer Res. 2008;28(2B):1417-20. PMid:18505089.
9. Prat J. Ovarian carcinomas, including secondary tumors: diagnostically challenging areas. Mod Pathol. 2005;18(Suppl 2):S99-111. http://dx.doi.org/10.1038/modpathol.3800312. PMid:15492758.
10. Lionetti R, De Luca M, Travaglino A, et al. Prognostic factors in Krukenberg tumor. Arch Gynecol Obstet. 2019;300(5):1155-65. http://dx.doi.org/10.1007/s00404-019-05301-x. PMid:31542818.

Authors' contributions: Lyngdoh BS and Dey B were involved in the histopathological workup of the resected specimen. Mishra J and Marbaniang E reviewed the case and made the diagnosis. Dey B and Lyngdoh BS wrote the article, which was reviewed and revised by Mishra J and Marbaniang E. All authors collectively proofread the final version and approved it for publication.

The authors retain informed consent signed by the patient, authorizing the data publication.

Conflict of interest: None

Financial support: None

Submitted on: February 7th, 2020

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